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Modern Concepts of Cardiovascular Disease

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CARDIOVASCULAR MANIFESTATIONS OF BERIBERI

Beriberi is a deficiency disease of nutritional origin. Like all nutritional deficiency diseases in man, it seldom results from lack of a single substance. Man rarely chooses or utilizes his food so that it is deficient in only one factor. The possible modifying influence of simultaneous deficiencies on the human body often prevent analysis of the effects of deficiency of a single substance under controlled conditions. This is one reason that deficiencies acutely induced in animals often differ from human defiiciency diseases.

The evidence available indicates that beriberi is caused *primarily* by deficiency of vitamin B_1. Patients with beriberi, nevertheless, often suffer simultaneously from deficiency of protein, calcium and iron, as well as from deficiency of other vitamins, as indicated by bodily changes corresponding to the lack of these substances.

Beriberi has been known for centuries as a devastating disease of the rice-eating people of the Orient. Subsequently it has been observed in other parts of the world. The "dry" form of the disease manifests itself mainly in muscle wasting and in neuritis; the "wet" form is associated with cardiovascular disturbances and edema. Psychotic manifestations often accompany either form of the disease. Recent studies indicate that the disease occurs in the United States, both in alcoholic and in nonalcoholic patients. Unbalanced diet or poor utilization of food, such as occurs at times in patients with peptic ulcer, chronic diarrhea, diabetes, pregnancy, thyrotoxicosis, infectious diseases and psychotic aberration ("food cranks"), is apt to predispose to the disease.

The term "beriberi heart" is not appropriate for the designation of the circulatory disturbances of the disease, because the circulatory dysfunctions depend on disturbance both of the peripheral vessels and of the heart. As a matter of fact, in the United States changes occur more frequently in the peripheral circulation than in the heart.

Clinical Characteristics. A comparison of the clinical characteristics of the disease in the United States with those reported in the Orient indicates that the disease here is similar, if not identical, to that in the Orient. Variations in the syndromes, however, have been greater in the United States.

The acute form of the disease is often precipitated by an increase in the requirement rather than by a decrease in the intake of vitamin B. The vitamin requirement is increased in conditions associated with a high metabolic rate of the body, such as fever, exercise and a high caloric intake of food. It is for this reason that persons with faulty nutrition and low vitamin B_1 intake but without symptoms ("presymptomatic" or "subclinical" beriberi) are apt to develop fulminating beriberi following severe exertion, or after the onset of malaria, pneumonia, typhus, dysentery and the like. It is probable that the high mortality rates of alcoholic patients suffering from pneumonia depend in part on nutritional deficiencies.

As the combination of high metabolic rate and low vitamin B intake particularly predisposes to the disease, patients with beriberi may be well nourished. This is particularly apt to be the case among the alcoholic group, who, as a result of the consumption of a large amount of alcohol, have a high caloric but low vitamin B intake.

The onset of the cardiovascular disturbance may be gradual or sudden. Dyspnea on exertion associated with palpitation, tachycardia and embryocardia are the early or the mild manifestations of the disease. Gallop rhythm, prominent cardiac and epigastric pulsations and bounding peripheral arterial pulses with sounds ("pistol shots") are also frequently present. The heart, on percussion and on Roentgenray examination, is found to be normal in size or enlarged; systolic and, rarely, diastolic murmurs are heard. In case of severe disturbance of the cardiovascular system the patient may appear anxious, restless, dyspneic, orthopneic, and the eyes may be slightly prominent. In severe cases the dyspnea is intense, particularly on exertion, and may appear with unexpected severity in previously robust individuals. Cardiac asthma (paroxysmal dyspnea) is present in a small number of cases. Signs of pulmonary congestion occur and roentgenological examination reveals cloudiness of the lung fields. The arterial pressure is usually normal, with a tendency to increased pulse pressure. In some of the patients the systolic pressure is moderately elevated, but this returns to normal with improvement. The veins of the neck are often engorged and the venous pressure is elevated. Frequently the veins are prominent over the lower extremities. The liver may be enlarged and tender. In the alcoholic group cirrhosis is often present. The skin is usually warm and of normal color; at times it is cyanotic. Edema is present in one group and may be severe and extensive. It is either diffuse or is a combination of the dependent and nondependent types. At times the edema is nonpitting, interstitial, and so generalized that the patient appears to be a robust individual when seen first. Only the intense diuresis and loss of 20 to 50 pounds following rest and medication reveals the nature of the generalized swelling of the body. Patients with beriberi cardiovascular disease tend to develop vasomotor collapse and shock. They also tend to develop bronchopneumonia. Fever particularly predisposes to circulatory collapse in this disease and is therefore of grave prognostic significance. These patients are poor surgical risks.

Patients with severe polyneuritis, like those described in the Orient, are not apt to suffer from severe cardiovascular disturbances. The inability to walk and work acts as a safety factor. Contrariwise, patients with a moderate degree of cardiovascular disturbance may be made worse by moderate exercise.

During improvement, diuresis and a change from tachycardia to transient bradycardia, often associated with overactivity of the vagus nerves (hyperactive carotid sinus reflexes), often precede changes in the venous engorgement, dyspnea and reduction of the cardiac size. Patients with beriberi cardiovascular disease often present symptoms and signs of noncirculatory nature. Some of them are part of beriberi; others depend on associated deficiencies. The most common of these are a sensation of lameness and "tightness" of the muscles of the lower and at times of the upper extremities, paresthesias,

peripheral neuritis, glossitis, constipation or diarrhea, dermatitis (pellagra), psychosis, anemia, hypoproteinemia, optic neuritis, dysphagia, hoarseness, aphasia, "spooned" nails and purpura (scurvy).

Physiology. The electrocardiogram often reveals changes, the most common findings being depression and inversion in the T waves and prolongation of the electric systole. At times low voltage of the electric complexes, premature auricular or ventricular beats and auricular tachycardia are observed. The vital capacity of the lungs is often severely reduced, and in spite of the increased venous pressure the velocity of the blood flow is relatively or absolutely increased. This increase in blood flow in the presence of heart failure is explained by the fact that the peripheral arterioles are in a dilated state. This is also attested by the small oxygen utilization by the tissues of the extremities. Thus the hemodynamics in beriberi cardiovascular disease are not unlike those in arteriovenous aneurysm, in thyrotoxicosis and in fever. In contrast to thyrotoxicosis and fever, however, the basal metabolic rate is not elevated. The edema of beriberi depends partly on increased capillary pressure resulting from arteriolar dilatation, partly on moderately or severely reduced osmotic pressure as a result of hypoproteinemia, and partly on other factors at present unknown. The severe edema per se may further accentuate the circulatory disturbance.

"Beriberi heart" in the past has been characterized mainly as right-sided failure. This right-sided failure has been attributed to the increased blood flow to the right ventricle. The nature of the hemodynamics, in harmony with the clinical observations, indicates that the disease as observed in the United States does not form a rigid clinical syndrome. Right ventricular failure, left ventricular failure, peripheral circulatory collapse and shock, singly or in various combinations, have been observed. The sequence of events and the causal interrelation in the development of the circulatory disturbances of beriberi are not well understood.

Wenckebach and Aalsmeer have observed that in patients with beriberi cardiovascular disease the circulatory difficulties are aggravated by the administration of epinephrin and temporarily improved by pituitary extract or pitressin. Such responses in our experience have not been regular.

Morbid Anatomy. In the Orient the morphological changes of the heart have been mainly characterized by dilatation of the right chambers of the heart. Our experience with postmortem examinations on patients has revealed that in the majority of instances the weight of the heart was normal and that there was dilatation of the right ventricle. In a small percentage of instances the cardiac weight was increased and all chambers of the heart, particularly the right ventricle, were dilated.

The histological changes observed in cases occurring in the United States are identical with those described by Wenckebach. Hydropic degeneration of the myocardial and conducting fibres, swollen collagen, perivascular "edema" and separation of the myocardial bundles are present. These changes, however, in our experience are not regular, nor are they specific for or characteristic of beriberi. It is of interest that the water content of the left and right ventricles is the same in cases of beriberi (including hearts with extensive perivascular "edema") as in normal persons or in patients with organic disease. This suggests that the accumulated intercellular substances contain an amount of solids similar to that in other tissues. Hence the heart in beriberi can develop structural changes from the initial chemical disturbances.

Differential Diagnosis. The clinical characteristics of the cardiovascular changes in beriberi, as in other cardiovascular diseases, are not specific. The characteristics of the disease, together with the absence of the etiology of other types of heart disease, permit, nevertheless, a diagnosis with a fair degree of probability. If a patient with severe alcoholism or with grossly abnormal nutritional history suddenly develops circulatory embarrassment in the presence of nonvalvular heart failure, bounding arterial pulse, peripheral arteriolar dilatation and diffuse interstitial edema with firm, prominent muscles, beriberi should be considered. The presence of other manifestations of nutritional deficiency disease, particularly polyneuritis, gastrointestinal disturbances, pellagroid skin lesions and a tendency to psychosis, will make the diagnosis probable. The precipitating effect of conditions associated with high metabolic rate should be taken into consideration. In the differential diagnosis the ruling out of certain obscure and rare myocardial diseases ("Fiedler's myocarditis," myocarditis of pregnancy) and coronary diseases may offer difficulty. The response to therapy resulting in complete recovery should be considered as a diagnostic test.

In the presence of organic heart disease the diagnosis of an element of beriberi cardiovascular disease is particularly difficult. The role of nutritional deficiency in organic heart disease cannot be evaluated at present. This will be possible with greater accuracy only when chemical or biological tests for vitamin B_1 are available.

Treatment. The response of the cardiovascular system in beriberi is not uniform. Some patients show improvement as a result of bed rest. Others, on the other hand, show unexpected aggravation of the disease, including vasomotor collapse, when kept in bed either on a vitamin B_1 deficient diet or on a balanced diet. Some of the patients show improvement and copious diuresis after the administration of mercurial diuretics and digitalis. In our experience the beneficial response was most regular when vitamin B_1 was administered parenterally, or when food and extracts rich in vitamin B_1 were given by mouth. Improvement was observed even if patients were kept on a special diet relatively free of B_1, and the sole therapeutic agent was crystalline B_1. The amount of vitamin B_1 injected varied between 5 and 20 milligrams of freshly prepared solution three or four times daily. The dosage was determined empirically. Because we do not as yet possess adequate information on the vitamin requirement and the storage of vitamin B_1, no rational basis exists for the estimation of the minimal effective dose. Beneficial responses were observed following oral administration of extracts rich in vitamin B_1. Because patients with beriberi often suffer from *gastrointestinal* and *liver* disorders which may well interfere with the *utilization* of vitamin B_1, it is advisable to use vitamin B_1 parenterally in acutely sick patients and to change to the oral method after the onset of improvement. The rate of improvement varies in different patients. Some patients improve rapidly within a week; in others, improvement is slower and recovery may take from four to six weeks or longer. Rapid improvement is usually associated with diuresis, bradycardia and temporary elevation in the arterial pressure. The variations in the histological changes of the myocardium are in harmony with such variations in the rate of response. In patients with both cardiovascular and nervous disturbances, improvement was usually more rapid and more complete in the cardiovascular system than in the nervous system. At times, however, the accompanying psychosis cleared rapidly. In persons with no deficiency, with or without organic heart disease, even massive doses of vitamin B_1 fail to exert any detectable effect on the cardiovascular system, so far as we know. Similarly, in our experience edema of nondeficient origin is not affected by vitamin B_1.

Because patients with beriberi often have other types of deficiencies, attention should be paid to the simultaneous treatment of pellagra with nicotinic acid and with vitamin B_2, of anemia with iron and with liver extract, of hypoproteinemia with a high protein diet, and of hemorrhagic tendencies with ascorbic acid.

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